08/869,386

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/869,386	06/05/97	SASTRY J	UTXC:538/HYL

EXAMINER: SMITH, I

HM11/0224

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ART UNIT	PAPER NUMBER
1648	7

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 10/2/97

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 29-48 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 29-48 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-421-632/40206

1. The examiner acknowledges the preliminary amendments canceling claims 1-28, adding claims 29-48 and amending claims 29-48. Claims 29-48 are pending and under consideration.

2. A substitute specification is required because the amendments to the specification requested by applicant are too numerous and will not be entered. The substitute specification filed must be accompanied by a statement that it contains no new matter. Such statement must be a verified statement if made by a person not registered to practice before the Office.

3. Claims 29 and 48 appear duplicative.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 46 and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to a method for inhibiting HIV infection of a cell in a human subject comprising injecting the composition comprising the claimed peptides. The examiner is interpreting the claims to read on a method of vaccinating a human subject against HIV infection.

The specification provides no probative evidence to support the claimed utility of a vaccine which would protect humans against AIDS. The obstacles to vaccine development and therapeutic

approaches with regard to retroviruses associated with AIDS in humans are well documented in the literature. These obstacles include: 1) the extensive genomic diversity associated with the HIV retrovirus, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to "hide" in the central nervous system where blood cells and neutralizing agents carried by the blood cannot reach the retrovirus, due to the blood-brain barrier and 5) the complexity and variation of the elaboration of the disease. The existence of these obstacles establish that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any vaccine or any immunization treatment or any therapeutic regimen on its face. In order to enable claims to drugs and their uses, either in vivo or in vitro data, or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the proposed claims are sufficiently enabled. When the claims are directed to humans adequate animal data would be acceptable in those instances wherein one of ordinary skill in the art would accept the correlation to humans. Thus in order to rely on animal data there must exist an art-recognized animal model for testing purposes. By definition vaccines must not only induce an immune response, but must be immunogenic to the extent that upon subsequent challenge with the live virus, development of the disease is prevented, or better yet infectivity does not occur. The specification appears to describe the generation of antibody responses and CTL responses in

mice to the peptides. However, the specification appears to lack evidence showing a correlation between that which occurs in mice and that which one would reasonably expect to occur in humans.

Additionally, with respect to the development of antibody responses and/or CTL responses, it is generally accepted that neither correlate with immunity to HIV (see Cohen and Butini, copies are enclosed). Finally, Fox (copy attached) has reported on the frustrations of AIDS researchers who attended the First National Conference on Human Retroviruses and Related Infections, and their attempts to develop a vaccine against HIV. It was generally agreed that 'No therapy has emerged as a sure winner in the campaign against HIV, not a preventive nor a therapeutic vaccine nor any of the immune-system-boosting treatments.".

Factors to be considered in determining whether a disclosure would require undue experimentation have been reiterated by the Court of Appeals in In re Wands, 8 USPQ d. 1400 at 1404 (CAFC 1988). In the instant application, 1) there are no working examples which suggest the desired results of a vaccine against HIV infection, 2) the nature of the invention involved the complex and incompletely understood area of immune parameters to HIV disease, 3) the state of the prior art shows that prior vaccines and treatment therapies have been largely ineffective for the intended purpose, 4) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level), and 5) the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by prior vaccine and treatment failures. Therefore, in view of all of the above and in view of the state of the art with respect to vaccines against HIV infection, it is

determined that it would require undue experimentation of one of skill in the art to use the invention for in vivo inhibition of HIV infection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 29-45, 48 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Haynes et al, U.S. Pat. No. 5,013,548. The claims are drawn to methods of inhibiting HIV infection of a cell comprising administering the claimed peptides comprising the claimed amino acid sequences. The examiner is interpreting the claims to read on an in vitro method.

Haynes et al teach methods of immunizing animals including mammals, comprising administering peptides comprising the claimed amino acid sequences. The peptides may be conjugated to larger molecules, may include one or more sequences from different isolates or the same isolate, may include spacer molecules (abstract, columns 5-12, tables 1-4). The steps in the method are the same as the steps in the claimed method and the peptides of Haynes et al comprise the claimed amino acid sequences. The peptides would inherently contain a surfactant like micelle upon conjugation to a spacer molecule. This essentially describes the invention as claimed. While Haynes et al do not specifically describe a method of inhibiting HIV infection, it is shown that administration of the peptides inhibits syncytia formation (table 4). Therefore, in the alternative, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the peptides to animals including mammals as taught by Haynes et al. It would have been expected, barring evidence to the contrary, that the peptides would generate immune responses which would inhibit syncytia formation and result in an inhibition of HIV infection. The conjugation of spacer molecules, the addition of cysteines to either the N-terminus or C-terminus of the peptide

and the administration of peptides in the claimed dosages are all well within the level of skill in the art and would be a matter of design choice.

7. Claims 29-33, 41 and 48 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Takahashi et al, 1989. The claims are drawn to a method of inhibiting HIV infection of a cell comprising administering peptides comprising the claimed amino acid sequences in a pharmaceutical carrier.

Takahashi et al teach a peptide which comprises the claimed amino acid sequence which peptide was involved in recognition of cytotoxic T cells (pages 2024-2029, figures 1-3). The peptide is the same as the claimed peptide. In the alternative, while Takahashi et al do not specifically describe a method of inhibiting HIV infection, it is stated that the peptide is an epitope for cytotoxic T cells. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the peptide as taught by Takahashi et al. It would have been expected, barring evidence to the contrary, that the peptide would generate CTL responses when administered, thus being effective in inhibiting HIV infection.

8. Since the Office does not have the facilities for examining and comparing applicants' method with the method of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed method and the method of the prior art (i.e., that the method of the prior art does not possess the same material structural and functional characteristics of the claimed method). See In re Best, 562 F.d. 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Lynette F. Smith, Art Unit 1648 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1648 FAX telephone number is (703)-305-4242. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Lynette F. Smith whose telephone number is (703) 308-3909.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Donald E. Adams, can be reached on (703) 308-0570.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SMITH/lfs
February 13, 1998

L. F. Smith

LYNETTE F. SMITH
PRIMARY EXAMINER
GROUP 1800